

What is claimed is:

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1. A method of administration of an active ingredient to a mammal through a transmucosal route, said method comprising:

a. delivering said active ingredient to a desired site in a body of said mammal; and, sequentially, at said desired site,

b. promoting dissolution of said active ingredient,

c. promoting absorption of said active ingredient.

2. The method of claim 1, wherein said active ingredient is delivered in a dosage form having a first portion and a second portion;

said step of promoting said dissolution comprising releasing said first portion of said dosage form;

said step of promoting said absorption comprising releasing said second portion of said dosage form.

3. The method of claim 2, wherein said desired site is selected from the group consisting of a site of administration and a site of absorption.

4. The method of claim 2, wherein said first portion includes one or more first substances that promote said dissolution of said active ingredient, said one or more first substances selected from the group consisting of pH-

adjusting substances, surface-active compounds, pharmaceutically-acceptable solvents and enveloping additives;

said second portion including one or more second substances that promote absorption, said one or more second substances selected from the group consisting of pH-adjusting substances, effervescent penetration enhancers, non-effervescent penetration enhancers and bioadhesives.

5. The method of claim 2, wherein said first portion of said dosage form includes a first pH-adjusting substance thereby said active ingredient attains a first state of dissociation that promotes dissolution;

said second portion of said dosage form including a second pH-adjusting substance thereby said active ingredient attains a second state of dissociation that promotes absorption.

6. The method of claim 5, wherein said first and said second pH-adjusting substances are respectively an acid and a base.

7. The method of claim 5, wherein said first and said second pH-adjusting substances are respectively a base and an acid.

8. The method of claim 5, wherein said first and said second pH-adjusting substance are respectively a base and a base.

9. The method of claim 5, wherein said first and said second pH-adjusting substances are respectively an acid and an acid.

10. The method of claim 1, wherein said transmucosal route is selected from the group consisting of buccal, sublingual, gingival, gastrointestinal, rectal, vaginal, and nasal routes.

11. The method of claim 1, wherein said active ingredient is selected from the group consisting of analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, laxatives, anorexics, antihistamines, antiasthmatics, antidiuretics, antifatulents, antimigraine agents, antispasmodics, sedatives, antihyperactives, antihypertensives, tranquilizers, decongestants, beta blockers, peptides, proteins, and oligonucleotides.

12. The method of claim 5, wherein said dosage form includes means for sequential release of said first portion and said second portion, said means for sequential release selected from the group consisting of coatings, membranes, matrix materials, pre-cursors of active ingredients and pre-cursors of pH-adjusting substances.

13. The method of claim 5, wherein said second portion of said dosage form comprises said second pH-adjusting substance dispersed in a controlled release matrix material.

14. The method of claim 5, wherein said first portion of said dosage form includes said active ingredient.

15. The method of claim 5, wherein said second portion of said dosage form comprises said second pH-adjusting substance surrounded by a coating, whereby said first pH-adjusting substance is peripheral to said coating in said dosage form.

16. The method of claim 15, wherein said active ingredient is peripheral to said coating in said dosage form.

17. The method of claim 5, wherein said second portion of said dosage form includes said second pH-adjusting substance surrounded by a membrane, said first pH-adjusting substance being peripheral to said membrane.

18. The method of claim 17, wherein said active ingredient is peripheral to said membrane in said dosage form.

19. A method for administering an active ingredient via a transmucosal route in a mammal, comprising administering said active ingredient in a dosage form with a first pH-adjusting substance and a second pH-adjusting substance so that said first pH-adjusting substance attains peak activity in the localized environment of the active ingredient before said second pH-adjusting substance attains peak activity in the localized environment of the active ingredient, whereby the localized environment of the active ingredient attains a first pH and then a second pH, said first pH promoting dissolution of said active ingredient and said second pH promoting absorption of said active ingredient.

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FOOTNOTES: 20, 22, 23, 24, 25, 26

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20. The method of claim 19, wherein said first and said second pH-adjusting substances are respectively an acid and a base.

21. The method of claim 19, wherein said first and said second pH-adjusting substances are respectively a base and an acid.

22. The method of claim 19, wherein said first and said second pH-adjusting substance are respectively a base and a base.

23. The method of claim 19, wherein said first and said second pH-adjusting substances are respectively an acid and an acid.

24. The method of claim 19, wherein said transmucosal route is selected from the group consisting of buccal, sublingual, gingival, gastrointestinal, rectal, vaginal, and nasal.

25. The method of claim 19, wherein said active ingredient is selected from the group consisting of analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, laxatives, anorexics, antihistamines, antiasthmatics, antidiuretics, antifatulents, antimigraine agents, antispasmodics, sedatives, antihyperactives, antihypertensives, tranquilizers, decongestants, beta blockers, peptides, proteins, and oligonucleotides.

26. The method of claim 19, wherein said administering step includes providing said second pH-adjusting

substance dispersed in a controlled release matrix material in said dosage form.

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27. The method of claim 25, wherein said active ingredient is peripheral to said controlled release matrix material in said dosage form.

28. The method of claim 19, wherein said administering step includes providing said second pH-adjusting substance surrounded by a coating, wherein said first pH-adjusting substance is peripheral to said coating in said dosage form.

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29. The method of claim 28, wherein said active ingredient is peripheral to said coating in said dosage form.

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30. The method of claim 19, wherein said administering step includes providing said second pH-adjusting substance surrounded by a membrane, wherein said first pH-adjusting substance is peripheral to said membrane in said dosage form.

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31. The method of claim 30, wherein said active ingredient is peripheral to said membrane in said dosage form.

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32. A pharmaceutical composition comprising an active ingredient in a dosage form comprising a first portion, a second portion and means for sequential release of said first portion and said second portion at desired site; said first portion including one or more first substances that promote dissolution of said active ingredient; said second

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cont portion including one or more second substances that promote absorption of said active ingredient.

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~~33~~. The composition of claim ³³~~32~~, wherein said first substance comprises a first pH-adjusting substance, said second substance comprises a second pH-adjusting substance, and said means for sequential release are means for sequentially controlling the activity of said pH-adjusting substances so that said first pH-adjusting substance attains peak activity in the localized environment of the active ingredient before said second pH-adjusting substance attains peak activity in the localized environment; whereby the localized environment of the active ingredient attains a first pH and then a second pH, said first pH promoting dissolution of said active ingredient and said second pH promoting absorption of said active ingredient.

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~~34~~. The pharmaceutical composition of claim ³⁴~~33~~, wherein said first and second pH-adjusting substances are respectively an acid and a base.

³⁶
~~35~~. The pharmaceutical composition of claim ³⁴~~33~~, wherein said first and said second pH-adjusting substances are respectively a base and an acid.

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~~36~~. The pharmaceutical composition of claim ³⁴~~33~~, wherein said first and said second pH-adjusting substance are respectively a base and a base.

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~~37.~~ The pharmaceutical composition of claim ³⁴~~33,~~
wherein said first and second pH-adjusting substances are
respectively an acid and an acid.

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~~38.~~ The pharmaceutical composition of claim ³³~~32,~~
wherein said means for sequential release are selected from
the group consisting of coatings, membranes, matrix materials,
active ingredients pre-cursors and precursors of pH-adjusting
substances.

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~~39.~~ The pharmaceutical composition of claim ³⁴~~33,~~
wherein said means for sequentially controlling the activity
of said pH-adjusting substances comprises at least one coating
that surrounds said second pH-adjusting substance, said first
pH-adjusting substance being peripheral to said coating in
said dosage form.

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~~40.~~ The pharmaceutical composition of claim ⁴⁰~~39,~~
wherein said active ingredient is peripheral to said coating
in said dosage form.

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~~41.~~ The pharmaceutical composition of claim ³⁴~~33,~~
wherein said means for sequentially controlling the activity
of said pH-adjusting substances comprises a controlled release
matrix material in said dosage form, said second pH-adjusting
substance being dispersed in said controlled release matrix
material, and said first pH-adjusting substance being
peripheral to said controlled release matrix material in said
dosage form.

~~42~~⁴³. The pharmaceutical composition of claim ~~41~~⁴², wherein said active ingredient is peripheral to said matrix material in said dosage form.

~~43~~⁴⁴. The pharmaceutical composition of claim ~~33~~³⁴, wherein said means for sequentially controlling the peak activities of said pH-adjusting substances comprises at least one membrane in said dosage form that surrounds said second pH-adjusting substance, said first pH-adjusting substance being peripheral to said membrane in said dosage form.

~~44~~⁴⁵. The pharmaceutical composition of claim ~~43~~⁴⁴, wherein said active ingredient is peripheral to said membrane in said dosage form.

~~45~~⁴⁶. The pharmaceutical composition of claim ~~32~~³³, wherein said active ingredient is selected from the group consisting of analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, laxatives, anorexics, antihistamines, antiasthmatics, antidiuretics, antifatulents, antimigraine agents, antispasmodics, sedatives, antihyperactives, antihypertensives, tranquilizers, decongestants, beta blockers, peptides, proteins, and oligonucleotides.

~~46~~⁴⁷. The pharmaceutical composition of claim ~~32~~³³, wherein said one or more first substances are selected from the group consisting of pH-adjusting substances, surface-active compounds, pharmaceutically-acceptable solvents and enveloping additives, said one or more second substances are

selected from the group consisting of pH-adjusting substances,
effervescent penetration enhancers and non-effervescent
penetration enhancers.

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